

# Discordant Deformity of Cleft Lip and Cleft Palate in Monozygotic Twins—a Case Report and Discussion.

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The twin method of studying the hereditary and environmental influences on developmental deformities is a well established method of investigation. This naturally occurring, controlled experiment may provide some of the answers to some of the problems associated with our growth development. Identical twins are not all that uncommon, but the recorded cases of proven identical twins with cleft lip and cleft palate deformity are not numerous enough to justify any conclusions being formed as to the etiology of this deformity. For this reason it is considered justifiable to report a pair of monozygous twins, one of whom suffers from cleft lip and cleft palate.

## Case Report

An African mother brought twin boys, age 6 months, to the Baragwanath Hospital, Johannesburg. These brothers on gross physical appearance (Figure 1) appeared to be identical twins. Yet, while one brother was normal, the other suffered from a complete unilateral cleft of the lip and the palate on the left side.

*Investigation of Zygosity.* (1.) The state of the birth membranes was not available. (2.) The gross physical appearance of twin boys appeared to be identical (Figure 1, 2). (3.) Detailed blood grouping was carried out and it was found that the twins had identical grouping for all 15 groups tested (Table 1). The maternal and paternal bloods were not available for testing. (4.) At the operation for the primary repair of the cleft lip deformity on the one twin, both twins were anaesthetised. A full thickness free skin graft was taken from behind the right ear of each twin and the skin was interchanged. The retro-auricular region of the twin who had the cleft palate repair shows a well healed, accepted skin graft some 10 weeks after grafting (Figure 3). The graft on the other twin had the same appearance at this time.

*Investigation of the Family History.* (1) The mother, by the same father, has three other male children, all of whom were normal single births. (2) The mother has four brothers and two sisters who are all

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TABLE 1. Blood grouping.

|                                   | <i>ABO</i> | <i>M</i> | <i>N</i> | <i>S</i> | <i>Kell</i> | <i>Fy<sup>a</sup></i> | <i>J<sub>s</sub></i> | <i>HEN</i> | <i>V</i> | <i>C</i> | <i>D</i> | <i>D<sup>u</sup></i> | <i>Le<sup>a</sup></i> | <i>Le<sup>b</sup></i> |
|-----------------------------------|------------|----------|----------|----------|-------------|-----------------------|----------------------|------------|----------|----------|----------|----------------------|-----------------------|-----------------------|
| Philip: cleft lip and palate..... | A1         | +        | +        | +        | —           | —                     | —                    | —(2+)      | —        | —        | —        | —                    | —                     | +                     |
| Philemon.....                     | A1         | +        | +        | +        | —           | —                     | —                    | —(2+)      | —        | —        | —        | —                    | —                     | +                     |

normal. (3) The father has four brothers and four sisters who are all normal. (4) In the mother's family tree there are three known pairs of twins who were normal. (5) In the father's family tree there is one known pair of twins who were normal. (6) None of the grandparents, aunts or uncles showed any congenital abnormality or physical deformity.

*Investigation of this Twin Pregnancy.* (1) The mother has suffered one previous miscarriage at two month's gestation. (2) The mother cannot recall being ill during the period of her pregnancy with these twins. (3) The mother took no drugs, medicines or African nature herbs during this pregnancy. (4) The delivery of these twins was apparently normal at the Discoverers' Hospital, Discovery, Transvaal, South Africa.

*The Repair of the Left Complete Cleft of the Lip.* This was repaired using the triangular flap as reported by Randall (15). A photograph taken some four weeks after the repair shows the close physical resemblance between these twins (Figure 2).

### Discussion

Price (13) states "the crux of the twin method of studying hereditary—environment problems is, in principle, sound enough. It is the assump-

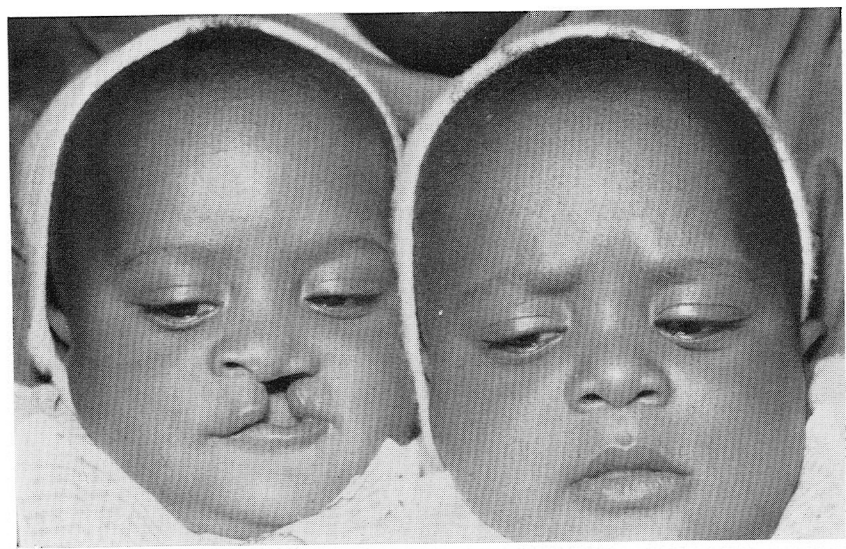


FIGURE 1. Pre-operative photograph of identical twins.



FIGURE 2. Taken four weeks following repair of cleft lip.

tion that monozygous twins are 'experiments' which nature has conducted for us, starting in each case with identical sets of genes and varying environmental factors. However we are after—the—fact observers of the results, and are left to guess what environmental factors nature put into the experiment."

As Metrakos et al (8) have so ably pointed out, the starting point of deduction in the twin method of studying hereditary environmental problems is to decide whether the twins are monozygous (i.e. arising from a single ovum fertilized by a single sperm) or dizygous. This diagnosis may be difficult and is based in all cases on a degree of probability.

Physical appearance supported by measurements of the height, weight, hair texture, skin color, iris color, and ear shape have been accepted in the past as adequate criteria to establish zygosity of twins. These gross measurements have quite a high percentage of error.

Further physical characteristics that may be more accurately measured and recorded such as dental patterns (17), finger print patterns (6, 19), cephalometric measurements (12) and determination of blood groups (16), have helped to reduce this chance of error in determining the zygosity of twins, but there remains a definite number of patients in whom the diagnosis is uncertain.

It is agreed that if babies are born with monochorionic membranes, whether they are mono-amniotic or di-amniotic, they must be monozygous twins. Steiner (18) has shown that with all other combinations of the fetal membranes, zygosity of the twins is uncertain.

Reciprocal homografting (a term used by Metrakos et al (8) to describe

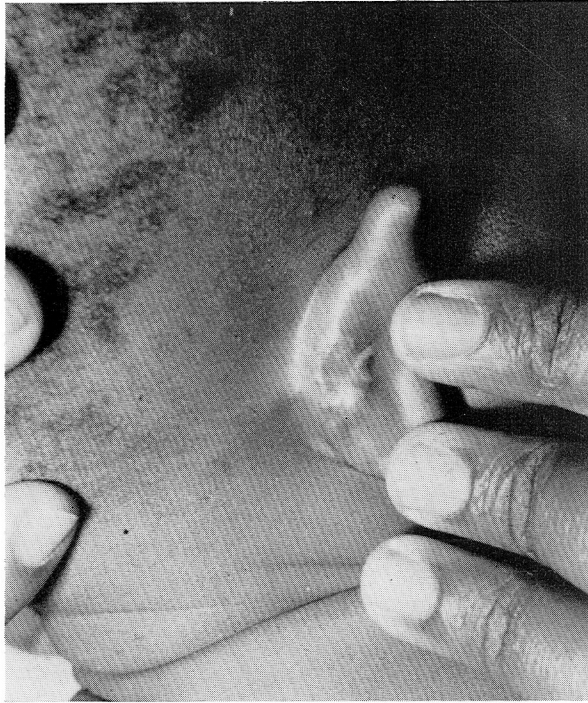


FIGURE 3. Healthy crossed post-auricular free skin graft ten weeks after transfer.

homografts between identical twins) is possible as the patients are at least genetically similar enough for their proteins to be histo-compatible. This phenomenon was first described by Bauer (1) in 1927 but was probably made more famous by the medico-legal identification of identical twins by McIndoe and Franceschetti (9) in 1950. This procedure, too, may not be absolute proof of monozygous twins, for successful reciprocal homografting may be carried out under the following rare conditions:

1. Where there has been chance genetic similarity.
2. Where genetic chimeras, as described in cattle by Ower (11), occur following cross circulation between dizygous twins who have a single placenta.
3. Where the patients may fail to produce adequate antibodies as in patients with agammaglobulinaemia (5).

These situations listed above, where reciprocal homografting may be successful between non-identical twins, are all so extremely rare that successful crossed homografting procedures, in the light of present knowledge, remain one of the best accepted criteria for the proof that twins are monozygous, or at least genetically similar enough for their proteins to be histo-compatible.

The question of positive proof of zygosity of twins may be difficult but one may postulate that where twins are found to have a single chorionic

membrane at birth or successful reciprocal homografting procedures have been performed, these twins are proven to be monozygous (or identical twins) as far as this is possible at the present time. Some of the earlier series of twin studies (4) have not adequately proven beyond reasonable doubt that all their patients regarded as identical twins have been in fact monozygous twins.

If one considers that twins must either be born with a single chorionic membrane or have had a reciprocal homograft procedure carried out before one can be certain that they are identical twins (monozygous) then as shown in Table 2, there are only ten sets of twins that I can find in the literature that fulfill these criteria and have cleft lip and/or cleft palate deformity. There is good evidence, first pointed out by Fogh-Andersen (4) in his monograph, that isolated cleft palate deformity is etiologically

TABLE 2. Details of cleft deformity in proven monozygotic twins.

| <i>author, year, reference</i> | <i>sex</i> | <i>mono-chorionic birth membranes</i> | <i>crossed skin graft</i> | <i>cleft lip</i> | <i>cleft palate</i> | <i>discordant/concordant abnormalities</i> |
|--------------------------------|------------|---------------------------------------|---------------------------|------------------|---------------------|--------------------------------------------|
| Brander, 1935, No. 4           | F          | +                                     |                           | —                | +                   | discordant                                 |
|                                | F          | +                                     |                           | —                | —                   |                                            |
| Steiner, 1935, No. 4           | F          | +                                     |                           | —                | +                   | discordant                                 |
|                                | F          | +                                     |                           | —                | —                   |                                            |
| Davis, 1922, No. 4             | F          | +                                     |                           | +                | +                   | concordant                                 |
|                                | F          | +                                     |                           | +                | +                   |                                            |
| Levy, 1928, No. 4              | M          | +                                     |                           | L                | —                   | concordant                                 |
|                                | M          | +                                     |                           | R                | +                   |                                            |
| Steiner, 1935, No. 4           | M          | +                                     |                           | +                | —                   | discordant                                 |
|                                | M          | +                                     |                           | —                | —                   |                                            |
| Metrakos, 1958, No. 8          | M          |                                       | +                         | R                | R                   | discordant                                 |
|                                | M          |                                       | +                         | —                | —                   |                                            |
| Ramsay, 1960, No. 14           | M          | +                                     | +                         | L                | L                   | concordant                                 |
|                                | M          | +                                     | +                         | R&L              | R&L                 |                                            |
| Boo-Chai, 1966, No. 2          | F          |                                       | +                         | L                | L                   | discordant                                 |
|                                | F          |                                       | +                         | —                | —                   |                                            |
| Boo-Chai, 1966, No. 2          | M          |                                       | +                         | R                | R                   | concordant                                 |
|                                | M          |                                       | +                         | L                | —                   |                                            |
| Youngleson, 1966               | M          |                                       | +                         | L                | L                   | discordant                                 |
|                                | M          |                                       | +                         | —                | —                   |                                            |

different from cleft lip deformity, with or without a cleft palate. Of the ten sets of twins presented, two sets have cleft palate deformity only, which are both discordant for this deformity. These have been separated from those patients with a cleft lip deformity.

Considering the eight sets of monozygous twins with cleft lip and/or cleft palate deformity, four of these twins were concordant for this abnormality. However the degree of development of the abnormality varied in three of these sets of twins. If one considers that identical twins are so similar they usually are indistinguishable physically then one would expect the development of the cleft lip and/or palate to be identical if this deformity was entirely genetically determined. It will be seen that of the four sets of twins who are concordant for the gross deformity three of these are discordant for the detailed analysis of the anatomical defect. There are many other isolated reports of patients who are "proven" identical twins but display a variety of discordant congenital anomalies.

The exact role of hereditary (the inheritance of physical characteristics to be determined by genes) and environment (intra-uterine) in the etiology of congenital deformities is not satisfactorily explained at the present time. The basic question of whether these congenital deformities are genetically determined, perhaps with varying degrees of penetration (10, 21, 20) is not decided. Some of the effects of alteration in the intra-uterine environment have been demonstrated experimentally (3) but the question as to why identical monozygous twins which probably have an identical intra-uterine environment can display discordant congenital anomalies is not satisfactorily answered at the present time (13). In fact Ivy (?) has published a photograph of a double headed male monster in which one face only has a complete unilateral cleft of the lip and palate.

## Summary

A pair of identical twins, proven by crossed free full thickness homograft skin transplantation, who were discordant for complete cleft lip and cleft palate deformity is presented. The relevant literature is reviewed.

Using the criteria of the state of the fetal membrane and crossed skin homografting procedure to prove that twins are monozygous, only ten pairs satisfying these criteria can be found in the literature. Of the ten pairs of monozygous twins, two sets suffered from isolated cleft palate deformity which was discordant in both pairs. Of the eight pairs of twins with cleft lip and/or cleft palate deformity four of these pairs were concordant for the abnormality.

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